REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Diseases in shrimp aquaculture have substantially reduced production and resulted in significant revenue losses. The use of molecular biology techniques to produce pathogen-resistant strains of shrimp through genetic transformation technology is considered a highly promising strategy for control of shrimp viral disease. In the past decade, pathogen-resistant transgenic animals and plants have been developed, but use of such technology has only just begun for shrimp research. While methods for detecting viral disease in shrimp, including polymerase chain reaction, light microscopy, and transmission electron microscopy, are widely used, methods for controlling viral disease in shrimp are still in development. One of the drawbacks to molecular engineering in shrimp and other crustaceans thus far has been the lack of a procedure to transform eggs or embryos with DNA that is easy, quick, highly efficient, and results in low mortality of eggs/embryos.

Three common methods of vector-expression for foreign nucleic acid delivery are electroporation, ballistic bombardment, and microinjection. Among these three methods, microinjection is considered to be the most tedious, but most efficient, method for transferring foreign nucleic acid into marine and fresh water species. It allows precision in delivery of exogenous nucleic acid and increases the chances that a treated egg will be transformed. The introduced nucleic acid is ultimately integrated into the chromosomes of the microinjected organism. Preston et al., "Delivery of DNA to Early Embryos of the Kuruma Prawn, *Penaeus japonicus*," *Aquaculture* 181:225-234 (2000), examined the relative efficiency of microinjection, electroporation, and particle bombardment for introducing nucleic acid into the embryos of the Kuruma prawn, *Litopenaeus japonicus* and found that microinjection is the most reliable technique but very time consuming. Electroporation is a desirable method for large scale gene transfer, however, host mortality tends to be high. An alternative non-surgical technique (e.g., spermatophore-microinjection), can be used as the delivery system, which provides somewhat better mortality. However, none of these methods of gene transfer is suitable to treat large numbers of fertilized shrimp eggs at one time, and most importantly, none of these methods raise the potential transformed shrimp into the mature stage.

Transgenic techniques provide a potential tool in producing shrimp capable of combating diseases and, subsequently, improving aquaculture production. However, at

present, transgenic shrimp studies suffer from the lack of availability of suitably efficient methods for the introduction of foreign DNA into the very fragile shrimp zygotes. What is needed is a method of *in vivo* DNA delivery into the eggs of shrimp and other that provides improved ease of use, improved efficiency of transformation, and improved mortality rates over the existing methods.

The present invention is directed to overcoming these and other deficiencies in the art.

The rejection of claim 1 under 35 U.S.C. § 101 for claiming non-statutory subject matter is respectfully traversed in view of the above amendments.

Claim 1 as amended is drawn to "[a] method of nucleic acid molecule delivery into a fertilized shrimp egg." Since the claims no longer encompass human eggs, the rejection under 35 U.S.C. § 101 is improper and should be withdrawn.

The rejection of claims 1-17 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed in view of the above amendments.

The outstanding office acknowledges that claims directed to "[a] method of nucleic acid molecule delivery into a fertilized shrimp egg," that involves "providing a fertilized shrimp egg prior to its formation of a protective layer; providing a nucleic acid molecule; and combining the nucleic acid molecule and the fertilized egg under conditions effective to allow the nucleic acid molecule to be delivered into the egg" are enabled by the present application. Since the claims have been amended so that they are limited to shrimp, the rejection of claims 1-17 under 35 U.S.C. § 112 (1st para.) for lack of enablement is improper and should be withdrawn.

The rejection of claims 1-2, 4, 6-7, 9, and 11-13 under 35 U.S.C. § 102(b) as anticipated by Tseng et al., "Introducing Foreign DNA Into Tiger Shrimp (Penaeus monodon) By Electroporation," *Theriogenology* 54:1421-1432 (2000) ("Tseng") is respectfully traversed.

Tseng teaches the electroporation of tiger shrimp fertilized eggs with a DNA expression vector, where the shrimp zygotes are collected 30 minutes after spawning and washed 2-4 times with buffer to remove the protective jelly coat layer. In contrast, the present invention claims a method of "providing a fertilized shrimp egg prior to its formation of a protective layer." Since Tseng does not teach all the limitations of the present invention, Tseng cannot anticipate the claimed invention.

Therefore, the rejection of claims 1-17 for anticipation by Tseng is improper and should be withdrawn.

The rejection of claims 1, 3, 5, 10, and 14-17 under 35 U.S.C. § 103(a) for obviousness over Tseng in view of Godbey et al., "Poly(ethylenimine) and Its Role in Gene Delivery," *Journal of Controlled Release* 60:149-160 (1999)("Godbey") is respectfully traversed.

A proper *prima facie* showing of obviousness requires the USPTO to satisfy three requirements. First, the prior art relied upon, coupled with knowledge generally available to one of ordinary skill in the art, must contain some suggestion which would have motivated the skilled artisan to combine or modify references. *See In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Second, the USPTO must show that, at the time the invention was made, the proposed modification had a reasonable expectation of success. *See Amgen v. Chugai Pharm. Co.,* 927 F.2d 1200, 1209, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Finally, the combination of references must teach or suggest each and every limitation of the claimed invention. *See In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). For the reasons below, the USPTO has failed to make a *prima facie* showing of obviousness.

Godbey teaches that polyethylenimine (PEI) is a cationic polymer that has been used to transfect human cell lines, as well as pig and rat primary cells *in vitro*, and newborn and adult mice and rats. Godbey does not teach or suggest "[a] method of nucleic acid molecule delivery into a fertilized shrimp egg." Even if Godbey were combinable with Tseng, which it is not, the combination of these references does not teach the claimed invention. In particular, the combination of Godbey and Tseng does not suggest utilizing a fertilized egg "prior to its formation of a protective layer." Thus, Godbey does not overcome the deficiencies of Tseng.

Moreover, Godbey states that "[i]ncreasing transfection efficiency while reducing toxicity must be accomplished before PEI can ultimately be used for efficacious gene therapies" (pg. 157, right col., last full para.). Thus, one skilled in the art would not have been motivated to combine the PEI transfection method of Godbey with the method of Tseng, nor would they have had a reasonable expectation of success in doing so.

For the reasons described above, the rejection of claims 1, 3, 5, 10, and 14-17 under 35 U.S.C. § 103(a) is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: November 10, 2005

Noreen L. Connolly
Registration No. 48,987

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1597
Facsimile: (585) 263-1600

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☒ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450

☐ transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) _____.

11-10-2005
Date

Angelica Grouse
Signature

Angelica Grouse
Type or Print Name